EPA Response to Fish Tissue-Residue Toxicity Reference Value Reconciliation Tables

General Comments

EPA has reviewed the Fish Tissue-Residue Toxicity Reference Value (TRV) Reconciliation Tables submitted to EPA on November 20, 2008 and the outcome of a meeting between representatives of EPA and the Lower Willamette Group (LWG) on December 16, 2008.

EPA has three primary areas of disagreement with the study exclusions and LOER modifications proposed by LWG in their reconciliation tables dated November 20, 2008:

1. EPA does not agree to exclude studies that measured tissue residues in sac-fry or larval stages of fish. The tissue TRV derivation methods state that only egg tissue residue-based studies should be excluded, and so LOERS based on tissue measurements in any fish life stage post-hatch (including sac fry) should be included for TRV derivation. Even though sac-fry will not bioaccumulate contaminants via dietary pathways, they clearly are capable of bioconcentrating contaminants from ambient water. Therefore, residue effects studies using sac-fry (or older life stages) should not be excluded from TRV development, so long as organisms are exposed via water or diet after hatching (i.e., the sac-fry are not exposed purely owing to maternal transfer or egg-only exposure).

2. EPA does not agree with many of the study exclusions on the basis of behaviors not being linked to survival, growth, or reproduction. For fish, EPA and its partners contend that the literature supports inclusion of studies using the following behaviors as being sufficiently linked to the assessment endpoints for fish receptors: locomotion (including swimming speed), predator avoidance, hypo or hyper activity, changes in temperature preference, and feeding. Attachment 1 to this document includes documentation of the relationship between predator-prey relationships, avoidance, feeding behavior and swimming and effects on survival, growth and reproduction.

3. EPA agrees to exclude studies in which positive growth (i.e., hormesis) was the basis for selection of the LOER. While hormetic responses are an inherent component of dose-response models for many chemicals, organisms, and endpoints (Calabrese 2008), EPA is unaware of any literature that demonstrates whether a positive growth response in laboratory fish can be linked to an “adverse” effect at the population level. Further, as stated in Van der Shalie and Gentile (2000), “It is impractical to apply hormetic effects to ecological risk-based benchmarks or criteria derived from distributions of species sensitivity data.” Consequently, EPA agrees that hormesis is not an appropriate response for use in developing TRVs for the BERA at Portland Harbor.

Study Specific Comments:

1. ***BEHP***. EPA reviewed this single study (Mehrle and Meyer 1976) in our original TRV submittal, and we recognize there are uncertainties with the interpretation of this study. Therefore, we agree to exclude this study as suggested by LWG.

2. ***Cadmium***. EPA agrees with all exclusions and modifications except for any related to the general comments above. Regarding the Pascoe and Mattey (1977) study, EPA identified a LOER of 0.9 mg/kg wet wt., while the LWG identified a LOER of 0.51 mg/kg wet wt. The note in the LWG table stated that they used the lowest reported measured residue in the experiment. The whole body (WB) Cd concentration of 0.51 mg/kg wet wt. reported in Table III of Pascoe and Mattey is based on the measured WB Cd concentration of 0.9 mg/kg wet wt. minus the control WB Cd concentration of 0.39 mg/kg wet wt. EPA used the WB Cd concentration of 0.9 mg/kg wet wt., which is consistent with the approach applied to other studies (i.e., EPA has not attempted to follow the "metal added" approach). Therefore, EPA retains our original interpretation of this study (LOER = 0.9 mg/kg wet wt.).

3. ***Chromium***. EPA agrees with all exclusions noted except for the mummichog study by Roling et al. (2006). EPA had cited a LOER of 44.1 mg/kg wet wt., which was based on a LOER of 220.6 mg/kg dry wt. divided by 5 (80% conversion). The LWG excluded this study because the LOER was based on embryos and the effect and exposure conditions were different. However, for the studies that elicited the LOER of 44.1 mg/kg ww, the exposure was initiated with larvae within 48 hours of hatching and exposed to Cr for 30 days. From our review of the study, exposure and effect conditions were from the same study, and so are a valid comparison using a valid life-stage (see general comment #1). Therefore, EPA recommends that this study be retained, thereby setting the TRV for chromium as the single remaining valid study.

4. ***Copper***. EPA agrees with all exclusions and modifications other than those related to the general comments above.

5. ***DDX***. EPA agrees with all of the suggested LOER modifications on the basis of ACR application because all study durations were greater than 30d. However, it should be noted that previous agreements do not allow for excluding ACRs if mortality levels are < 50%, so this language should be removed from this and all other tables. EPA agrees with all of the suggested exclusions except those related to the general comments above, and except for the exclusion of Berlin et al. (1981) lake trout study. Similar to the Broyles and Noveck (1979) PCB study discussed below, even though fish and eggs were obtained from a hatchery or were field collected in Lake Michigan, the study itself consisted of a valid experimental exposure of DDX to fry. Therefore, the LOER from Berlin et al. (1981) should be retained.

6. ***Mercury***. EPA disagrees with the different LOER proposed for the Heisingner et al. 1979 because upon closer examination, LWG used a dry weight-based LOER from Table 2 of this paper. However, EPA's originally proposed value was also in error, and recommends selecting the results relating to 35% mortality (4.4 mg/kg ww) which, when divided by the ACR, would derive a LOER of 1.18 mg/kg ww.
   EPA agrees with all exclusions except those related to the general comments above (e.g., Webber and Haines 2003 should be retained), and except for the exclusion of Matta et al. 2001. LWG excluded this study owing to use of anecdotal behavior responses, and mortality being a result of aggression, rather than Hg exposure. The study does indeed discuss the anecdotal behavioral responses, but this does not negate the valid empirical mortality results presented in the study in which a statistically valid dose-response between tissue Hg and mortality was observed. The LOER of 0.47 mg/kg ww from Matta et al. 2001 thus should be retained.

7. ***Lead***. There are no differences between EPA and LWG interpretations for this TRV, and so study inclusion/exclusions are acceptable as presented.

8. ***PCBs***. EPA agrees with all of the suggested LOER modifications except for the following:
   - Nebeker et al. (1974), fathead minnow. EPA disagrees that the female tissues should be preferentially selected over the male tissues, and so the more conservative male tissue-based LOER (196 mg/kg) should be retained. One of the most sensitive effects measured was in “spawning,” although it is unclear from a close examination of the manuscript whether spawning is defined as just deposition of eggs, or deposition and fertilization of eggs. EPA recommends using the latter interpretation because it does not make sense that a deposited, but unfertilized, egg would constitute a successful spawning event. Therefore, using the more conservative male tissue-based LOER is appropriate.

   EPA agrees with all of the suggested study exclusions except for those related to the general comments above, and for the following:
   - Broyles and Noveck 1979. EPA disagrees that this study should be excluded (for both Chinook salmon and lake trout). First, as in general comment #1, it is not appropriate to exclude studies conducted with post-hatch larval life stages. Second, EPA disagrees with the arguments articulated by LWG representatives in our December 16, 2008 meeting. Even though fish and eggs were obtained from a hatchery or were field collected in Lake Michigan,

the study itself consisted of a valid experimental exposure of PCBs in water to fry. Therefore, LOERs for both species from this study should be retained.

9. ***Zinc***. EPA agrees with all of the suggested LOER modifications and study exclusions except for those related to the general comments above, and the following specific studies:
   - Eisler and Gardner (1973), mummichog. Both LWG and ACR correctly applied an ACR to this study, in contrast to comments in the "notes" column. However, EPA made a calculation error in our original LOER selection, and upon closer examination of the original study, EPA now recommends an effects level of 1,266 mg/kg ww, which when divided by the ACR, gives an LOER of 633 mg/kg ww.
   - Pierson (1981), guppy. This study should be retained because the absolute changes in sex ratio reported in this study are significant enough to have a high likelihood of causing an impact on fish population reproduction.

References:

Calabrese, E.J. 2008. Hormesis: Why it is important to toxicology and toxicologists. Environ. Toxicol. Chem. 27(7):1451-1474.

Van der Schalie and Gentile, 2000. Ecological Risk Assessment: Implications of Hormesis. J. Appl. Toxicol. 20, 131–139.

Attachment 1: Relationship Between Certain Behavioral Endpoints and Survival, Growth and Reproduction.

Predator-prey relationships:

Weis et al. (2000) described how mummichog exposure to mercury affected their behavior (an organism level effect), and the behavioral alteration effects were linked to both biochemical level effects and population/community level effects. Fish exposed to mercury were found to have reduced condition, growth and longevity relative to that of unexposed controls. The observed growth and longevity reductions were due to mercury effects on the prey capture ability of mummichogs, which was reduced by mercury exposure. The detailed discussion of reduced prey capture behavior effects on growth and longevity begins on page 147 of this paper.

Avoidance behavior:

A good example here is a series of studies by John Sprague and coworkers with Atlantic salmon. The attached paper (Sprague et al. 1965) presents the combined results of laboratory and field studies that document surface water concentrations of copper and zinc actively avoided by Atlantic salmon, resulting in lowered egg production and young salmon population depression as a direct result of avoidance preventing adult salmon from reaching their spawning grounds and spawning. This demonstrates the effects of avoidance behavior on reproduction, as well as a population reduction in the field. Pages 532 and 533 give a discussion of the avoidance - population reduction linkage. Two other references to this group of studies (Sprague 1964, Saunders and Sprague 1967) are also given in the behavioral report.

Feeding behavior:

The Weis et al. 2000 paper mentioned under predator-prey behavior above also is a good example of how changes in feeding behavior can adversely affect survival and growth. Fish with reduced growth and longevity also had altered feeding patterns due to mercury exposure. Page 150 of Weis et al. 2000 describes the dietary shift of mercury exposed fish away from their normal diet of live prey that had to be actively caught to a detritus based diet not requiring active chasing and capture of prey. This is an alteration of feeding behavior. Alterations in feeding behavior are closely linked to observed changes in predator-prey relationships. A second example of altered feeding behavior effects on growth, is Buckley et al. (1982), starting on page 16, demonstrated long term reductions in growth of coho salmon due to reduced feeding during exposure to copper.

Swimming activity:

Smith and Weis (1997) exposed mummichogs to methylmercury, then made several behavioral observations, including on their overall swimming activity and subsequent vulnerability to predation. Mercury exposed mummichogs exhibited hypoactivity and reduced swimming activity, which led to a statistically significant increase in their vulnerability to predation by blue crabs (Table 3 presents the results, page 85 the discussion of this finding). Alteration of mummichog swimming activity by mercury directly led to increased mortality in this study.

References:

Buckley et. al., 1982. Chronic Exposure of Coho Salmon to Sub-lethal Concentrations of Copper. Effect on Growth, on Accumulation and Distribution of Copper and on Copper Tolerance. Comp. Biochem. physiol., Volume 72C, No. 1. pp 15-19.

Smith and Weis, 1997. Predator-prey relationships in mummichogs *(Fundulus heteroclitus* (L.)): Effects of Living in a Polluted Environment. Journal of Experimental Marine Biology and Ecology, 209: pp 75-87

Sprague et. al, 1965. Sublethal Copper Pollution in a Salmon River – a Field and Laboratory Study. Int. J. Air Wat. Poll. Volume 9: pp 531-543.

Weis et. al. , 2000. Predator/prey Interactions: A Link Between the Individual Level and Both Higher and Lower Level Effects of Toxicants in Aquatic Ecosystems. Journal of Aquatic Ecosystem Stress and Recovery 7: pp 145–153.